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(71) Applicant (for all designated States except US): **GLAXO-SMITHKLINE BIOLOGICALS S.A.** [BE/BE]; Rue de l'Institut 89, B-1330 Rixensart (BE).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **JACQUET, Alain** [BE/BE]; Universite Libre de Bruxelles, Institute de Biologie et de Medicine Moleculaire, Rue de Professers Jeener et Brachet 12, B-6041 Gosselies (BE).

(74) Agent: **RILEY, Victoria, Jayne**; GlaxoSmithKline (CN925.1), 980 Great West Road, Brentford, Middlesex TW8 9GS (GB).

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **HYPOALLERGENIC DER P 1 AND DER P 3 PROTEINS FROM DERMATOGRAPHOIDES PTERONYSSINUS**

(57) Abstract: The present invention provides a treatment for allergy comprising the provision of a recombinant Der p 1/ProDer p 1/PreProDer p 1 allergen derivative, ProDer p 3 or a recombinant ProDer p 3/Der p 3/PreProDer p 3 allergen derivative with hypoallergenic activity. Pharmaceutical compositions comprising said mutant allergens which stimulate a Th1-type immune response in allergic or naïve individuals thereby reducing the potential for an allergic response upon contact with the wild-type allergen, are also provided.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/001850

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K14/435 A61K38/43 C12N15/63 C12N9/64 C12N15/12
C12N5/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 01/96385 A (SMITHKLINE BEECHAM BIOLOG ; BOLLEN ALEX (BE); JACOBS PAUL (BE); JAC) 20 December 2001 (2001-12-20) the whole document	1, 3-14, 20-28, 30
Y	WO 02/074250 A (PANACEA PHARMACEUTICALS ; RABJOHN PATRICK A (US); BANNON GARY A (US) 26 September 2002 (2002-09-26) the claims and Appendix 4	1, 3-14, 20-28, 30
Y	WO 99/25823 A (SMITHKLINE BEECHAM BIOLOG ; BOLLEN ALEX (BE); JACOBS PAUL (BE); BRU) 27 May 1999 (1999-05-27) page 6, line 30 - page 9; claim 10 -/--	1, 3-14, 20-28, 30

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
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- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- *G* document member of the same patent family

Date of the actual completion of the international search

2 July 2004

Date of mailing of the international search report

06. 06. 2005

Name and mailing address of the ISA
European Patent Office, P.B. 5618 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Marinoni, J-C

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2004/001850

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	JACQUET ALAIN ET AL: "Conversion of ProDer p 1 into a mature Der p 1 is an autocatalytic processing which is dependent of the cysteine proteinase activity of the allergen" JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, vol. 107, no. 2, February 2001 (2001-02), page S16, XP009032859 57th Annual Meeting of the American Academy of Allergy, Asthma and Immunology; New Orleans, Louisiana, USA; March 16-21, 2001 ISSN: 0091-6749 abstract	1,3-14, 20-28,30
Y	SHAKIB F ET AL: "The proteolytic activity of Der p 1 selectively enhances IgE synthesis: A link between allergenicity and cysteine protease activity" CLINICAL AND EXPERIMENTAL ALLERGY 2000 UNITED KINGDOM, vol. 30, no. 6, 2000, pages 751-752, XP002286891 ISSN: 0954-7894 the whole document	1,3-14, 20-28,30
P,X	WO 03/016340 A (GLAXOSMITHKLINE BIOLOG SA ; BOLLEN ALEX (BE); JACQUET ALAIN (BE); M) 27 February 2003 (2003-02-27) the whole document	1,3-14, 20-28,30
A	WO 92/04445 A (WESTERN AUSTRALIAN RES INST) 19 March 1992 (1992-03-19)	
A	JACQUET A ET AL: "Absence of immunoglobulin E synthesis and airway eosinophilia by vaccination with plasmid DNA encoding ProDer p 1." CLINICAL AND EXPERIMENTAL ALLERGY, vol. 33, no. 2, February 2003 (2003-02), pages 218-225, XP002286892 ISSN: 0954-7894 (ISSN print)	

INTERNATIONAL SEARCH REPORT

national application No.
PCT/EP2004/001850

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 30
because they relate to subject matter not required to be searched by this Authority, namely:
Although claim 30 directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 3, 19
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1, 3-14, 20-28 and 30 partially

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1, 3-14, 20-28 and 30 partially

Hypoallergenic mutants of the Der p 1 protein of Dermatographoides pteronyssinus wherein cysteines have been mutated, nucleic acids encoding the same, vectors, methods and uses related thereto.

1.1. claims: 1, 3-14, 20-28 and 30 all partially

wherein the cysteine residue at position 71 has been mutated

1.2. claims: 1, 3-14, 20-28 and 30 partially

wherein the cysteine residue at position 103 has been mutated

1.3. claims: 1, 3-14, 20-28 and 30 partially

wherein the cysteine residue at position 117 has been mutated

2. claims: 2-14, 20-28, 30 partially

Hypoallergenic mutants of the Der p 1 protein of Dermatographoides pteronyssinus wherein amino acids 147-160 have been deleted (positions 227-240 of proDer p 1), nucleic acids encoding the same, vectors, methods and uses related thereto.

3. claims: 15-19, 29 completely; claims 20-28, 30 partially

Hypoallergenic mutants of the Der p 3 protein of Dermatographoides pteronyssinus wherein the protein has been either thermally treated or mutated (in particular at the positions corresponding to cystein residues), nucleic acids encoding the same, vectors, methods and uses related thereto.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claim 30 directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box II.1

Claims Nos.: 30

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

Continuation of Box II.2

Claims Nos.: 3,19

Claims 3 and 19 are directed to allergens having the sequences as set out in SEQ ID No. 15, 17 and 19. However, SEQ ID No. 15, 17 and 19 disclose oligonucleotides which cannot be regarded as allergens. It results that the claims are so unclear and their subject-matter is so unsufficiently disclosed that no search has been carried out for claims 3 and 19.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/001850

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